

To the Medical Profession

Scarlet Fever Toxin for the Dick Test

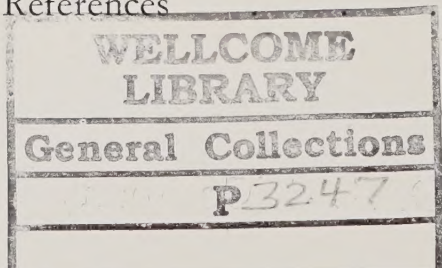
Scarlet Fever
Streptococcus
Antitoxin
for Treatment



Parke, Davis & Company

Scarlet Fever Toxin and Antitoxin

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Test of Susceptibility to and Treatment of Scarlet Fever

THAT means are now available for combating scarlet fever—means approaching in usefulness those which have been utilized so successfully in controlling diphtheria—seems to be assured by research developments of recent years.

Scarlet Fever Antitoxin is established as a useful agent both for the treatment of scarlet fever and for the temporary protection of susceptible individuals who have been exposed to the disease.

The Dick Test of susceptibility promises to be quite as useful in the control of scarlet fever as the Schick Test is in connexion with diphtheria. The physician and the public health authorities are thus afforded a basis for intelligently determining the necessity of adopting the use of Scarlet Fever Streptococcus Antitoxin for conferring temporary immunity, for example, in school children who may have been in contact with scarlet fever.

The use of Scarlet Fever Toxin has been suggested for prophylaxis, but sufficient work has not yet been done to determine its value for this purpose; there is, however, reason to believe that it may eventually become an effective measure of protection, and that lasting immunity will be conferred by the careful use of the toxin.

With these specific agents available, there seems ample reason to hope that the time is not far distant when this dread disease of child life will be robbed of most of its terrors.

Scarlet Fever Streptococcus Toxin

FOR USE IN THE DICK TEST

The Dick Test (for determining susceptibility to scarlet fever) consists of the intradermal injection of one skin test dose of Scarlet Fever Streptococcus Toxin, this amount of toxin being contained in 0.1 c.c.

In carrying out the test an accurate syringe with a short, but sharp-pointed, fine needle is necessary.

The injection may conveniently be made into the antero-internal surface of the forearm, the site being first carefully cleansed with soap and water, followed by a suitable disinfectant. The injection should always be made intradermally, not subcutaneously;

that is, the point of the needle must be introduced into the skin between the epidermis and the *cutis vera*, not under the latter. If the toxin is injected too deeply, escaping into the subcutaneous tissues, a positive reaction will not follow, even in those who are susceptible. When the injection has been carried out successfully, the epidermal layer is raised from the deeper layers of the skin and is sharply defined.

The reaction depends on the local irritant action of minute quantities of scarlet fever streptococcus toxin when injected intradermally. If there is no antitoxin in the blood of the individual undergoing the test, or if it is present in too small an amount to afford protection, a positive reaction will appear in twenty-four to forty-eight hours. This is characterized by a circumscribed area of redness and slight infiltration which measures 1 to 2 cm. or more in diameter, persists for a few days, and on fading shows a slight brownish pigmentation. In individuals immune to scarlet fever these signs do not appear.

When individuals who have recently been exposed to infection are found to be susceptible to scarlet fever passive immunity of a temporary character, lasting probably about ten days, may be conferred by the injection of Scarlet Fever Streptococcus Antitoxin.

Scarlet Fever Streptococcus Antitoxin

CONCENTRATED (GLOBULIN)

The development of Scarlet Fever Streptococcus Antitoxin, Concentrated (Globulin), represents a most important advance.

Based on the work of Tunnicliff¹, Dochez², the Dicks³, Zingher⁴ and others, relative to the etiological relationship of a certain type of the streptococcus hæmolyticus to scarlet fever, this serum is prepared according to a method perfected in the Medical Research Laboratories of Parke, Davis and Company⁵, as follows :

Horses are treated with gradually increasing doses of fresh live virulent cultures and toxic filtrates of Streptococcus hæmolyticus scarlatinæ isolated from the throats of patients suffering from scarlatina in a severe form.

As in the case of other therapeutic serums, the antitoxic or antibacterial principle (in this case both) is developed gradually in the blood of the treated animal ; and when the series of injections is completed the jugular vein of the horse is tapped and a quantity of blood withdrawn. This blood, on standing, separates into two parts, coagulum and serum, and the latter is syphoned off for further treatment.

The serum is then concentrated to the

globulin form according to accepted methods, and the sterility, safety and antitoxic potency of the product are controlled by procedures approved by the United States Public Health Service.

STANDARDIZATION

The standardization of Scarlet Fever Streptococcus Antitoxin is based on the ability of the product to neutralize scarlet fever toxin when injected intradermally into susceptible individuals. Methods for carrying out this test have been prescribed by the United States Public Health Service, the degree of activity required being that 1 c.c. of the serum should neutralize at least 1,000 skin test doses of toxin.

The antitoxin content of Scarlet Fever Streptococcus Antitoxin, Concentrated (Globulin), Parke, Davis and Company, is far in excess of this government stipulation. Each cubic centimetre neutralizes more than 35,000 skin test doses of scarlet fever toxin, and the product will be sent out in packages containing the standard dose in a volume not exceeding 10 c.c.

It has been demonstrated also that this serum will produce the diagnostic rash-fading reaction of Schultz-Charlton.

In addition to its high antitoxin content, this serum is actively antibacterial, as shown by agglutination and passive protection

tests ; thus it exerts a direct action on the infectious process as well as neutralizing the toxæmia.

CONCENTRATION

The concentration of the serum (which is accomplished by a method analogous to that utilized for the refinement of Diphtheria Antitoxin) reduces the size of the dose required, increases the potency of the product, and eliminates a large amount of objectionable protein. The refined product has the same advantages over unconcentrated scarlet fever serums as the globulin form of diphtheria antitoxin, now almost universally employed, possesses over the unconcentrated serum formerly used. The distressing skin reactions and other manifestations of "serum sickness," which have so often attended the clinical administration of unconcentrated serums, are reduced both in frequency and degree. Nevertheless there may be some urticarial serum rash, though in many cases it is quite trivial.

ADMINISTRATION

In the treatment of scarlet fever it is advisable to inject Scarlet Fever Streptococcus Antitoxin intramuscularly into the gluteal region in a dose of 10 c.c. as soon as the diagnosis is made. As reported by Gardner Robb⁷ and others the early use of the serum is of the utmost importance. If

the temperature and pulse do not show a decided drop within twenty-four to thirty-six hours a second injection is indicated.

The Antitoxin may be administered intravenously if the physician so elects ; one such case is referred to by Gardner Robb in the report mentioned above.

THERAPEUTIC RESULTS

The results which have followed the use of Streptococcus Scarlet Fever Antitoxin, not only in America but also in this country, have, in the great majority of cases, been very striking. Provided the serum is administered early in the disease the results would seem to be equally as satisfactory as those following the use of diphtheria antitoxin in cases of diphtheria. Only in rare instances does it appear to be necessary to administer a second dose.

Following an injection of the serum the fever generally subsides very rapidly, there are few or no complications, and as reported by Gardner Robb the quarantine period is considerably lessened. Thus, it is stated by this authority that they have released from isolation over 20 cases whose quarantine time from the onset of illness varied from seventeen to twenty-four days. It should be added, however, that the cases thus early released had come under treatment very early in the attack.

Desquamation is reduced ; if patients have had the serum early enough there is generally none. If administration of the serum is delayed for three days, or more, desquamation is slight.

PROPHYLACTIC VALUE

A limited investigation has been made of the prophylactic value of Scarlet Fever Streptococcus Antitoxin, Concentrated. The results so far reported indicate that doses of 2.5 c.c. administered to children ranging in age from 5 to 15 years are capable of changing a " Dick-positive " skin test to a " Dick-negative " one.

Further study is required in connexion with the prophylactic application of Scarlet Fever Antitoxin. While sufficient work has not yet been done to warrant final conclusions, the indication seems clear that children who have been exposed to scarlet fever, and who show a positive skin test (Dick reaction), should receive the 2.5 c.c. dose. The immunity following such an injection probably does not last more than about ten days, so that it is very important that exposed children should be removed from contact with scarlet fever patients.

SENSITIZATION TEST

Individuals in certain rare instances evince an extreme hypersensitiveness to the proteins in horse serum. For this reason it is

advisable to observe a few preliminary precautions to avoid, as far as possible, any untoward reactions that might occur.

For determining hypersensitiveness to horse serum, the intradermal test may be carried out with Scarlet Fever Streptococcus Antitoxin, Concentrated, by taking a fraction of a cubic centimetre directly from the bulb and diluting it with ten parts of sterile salt solution. About 0.2 c.c. of this is injected into the skin (not under the skin as with a subcutaneous injection) so that a small white wheal, about 3 mm. in diameter, is produced. An injection of a like amount of salt solution is given at the same time, as a control, a short distance from the first. If the patient is not sensitive to horse serum the wheal produced by the serum injected will fade away within a few minutes. If, on the other hand, sensitiveness does exist, an urticarial wheal will develop, surrounded by a zone of erythema. This reaction will reach its maximum in about one hour and then gradually fade away.

If the patient is found to be sensitive, it is advisable to begin the therapeutic use of the serum by the injection of 0.025 c.c. ($\frac{1}{3}$ minim) subcutaneously, and to double this dose every half-hour. If no reaction is observed after 1 c.c. has been injected, subsequent doses may be given intravenously, starting with 0.1 c.c. and doubling the dose

every half-hour until the desired amount has been injected. It is only necessary to resort to this long and tedious method in case the patient is sensitive to horse serum.

The above precautions are particularly important in the case of individuals who suffer from asthma, hay fever, or other conditions associated with protein sensitiveness, also in those who have previously been treated with horse serum, as, for instance, with diphtheria antitoxin.

Packages

Scarlet Fever Toxin for the Dick Test is supplied in a package consisting of two 5-c.c. vials, one of which contains undiluted toxin and the other 5 c.c. of diluent, the whole being sufficient for making fifty tests.

Scarlet Fever Streptococcus Antitoxin Concentrated (Globulin) is supplied in bulbs of 10 c.c., which is the dose for all cases, irrespective of age.

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